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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/768,371	01/30/2004	Igor Gonda	6809.230-US	6533

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EXAMINER	
LEWIS, AARON J	

ART UNIT	PAPER NUMBER
3743	

DATE MAILED: 12/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/768,371	GONDA ET AL.	
	Examiner	Art Unit	
	AARON J. LEWIS	3743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1,3-5,7-9,11-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laube et al. ('094) in view of Weiner et al. ('886).

As to claim 1, Laube et al. disclose a method of treating diabetes mellitus in a patient in need thereof, said method comprising: supplying a predetermined amount of insulin to a hand held device (14,col.4, lines 41-50), said predetermined amount being in excess of that amount required, in the bloodstream of the patient, to produce or maintain an acceptable serum glucose level in the patient (i.e. the amount in canister 14 and in jet nebulizer disclosed at col.4, line 42 includes enough insulin for several administrations which taken together exceed any amount required to produce or maintain an acceptable serum glucose level); contacting said insulin with a compressed gas to form a cloud in said hand held device (#30,#50,#70 and col.4, lines 46-50), said cloud comprising a repeatable amount of insulin (col.5, lines 1-12), said repeatable amount being in excess of that amount required, in the bloodstream of the patient, to produce or maintain an acceptable serum glucose level in the patient (col.5, lines 6-14); and inhaling said cloud at an inspiratory flow rate and volume (col.5, lines 53-55)

adapted to deliver a portion of said cloud to the lungs of the patient, wherein a controlled and reproducible amount of said insulin from the cloud is absorbed in the bloodstream of said patient to produce or maintain an acceptable serum glucose level; wherein the step of inhaling is repeated during a dosing event and wherein for each repetition of the inhaling step insulin administration to the patient begins at substantially the same inspiratory flow rate and inspiratory volume (col.5, lines 53-55).

The differences between Laube et al. and claim 1 are said cloud comprising insulin particles in the range between 0.25 and 6 microns and insulin being in powdered form.

Weiner et al., in a method of treating diabetes mellitus, teach the administration of insulin as a liquid or powdered aerosol (via well known nebulizers and metered dose inhalers) having particles sizes 1-5 microns (col.7, line 55-col.8, line 31). Accordingly, Weiner et al. establish a functional equivalency between liquid aerosol and powdered aerosol insulin.

It would have been obvious to employ the metered dose inhaler of Laube et al. to administer powdered insulin because liquid aerosol and powdered aerosols of insulin are functional equivalent forms of the medicament as taught by Weiner et al..

As to claim 3, Laube et al. as modified by Weiner et al. as discussed above also disclose mechanically supplying a predetermined amount of dry insulin powder to a given area (14,col.4, lines 41-50) of a hand held device, said predetermined amount being in excess of that amount required, in the bloodstream of the patient, to produce or maintain an acceptable serum glucose level in the patient (i.e. the amount in canister 14 and in jet nebulizer disclosed at col.4, line 42 includes enough insulin for several

administrations which taken together exceed any amount required to produce or maintain an acceptable serum glucose level); aerosolizing said insulin with a compressed gas to form a cloud in said hand held device (#30,#50,#70 and col.4, lines 46-50), said cloud comprising a repeatable and controlled amount of insulin, said repeatable and controlled (i.e. 0.2U/kg body weight) amount (col.5, lines 1-12) being in excess of that amount required, in the bloodstream of said patient, to produce or maintain an acceptable serum glucose level in the patient (col.5, lines 6-14); and inhaling said cloud at an inspiratory flow rate and volume (col.5, lines 53-55) adapted to deliver a portion of said cloud to the lungs of the patient, wherein an amount of insulin in said cloud effective, in the bloodstream of the patient, to produce or maintain an acceptable serum glucose level in the patient is absorbed into the bloodstream of the patient (col.5, lines 6-14). Weiner et al. teach insulin particle sizes of 1-5 microns which is within the claimed range of less than 12 microns. While Laube et al. is silent as to the particular pressure within the metered dose inhaler (14), it is submitted that the particular pressure can be arrived at through mere routine obvious experimentation and observation with no criticality seen in any particular pressure including 400psi. One or ordinary skill would recognize the need for safety when pre-pressurizing metered dose inhalers; accordingly, pressures less than 400psi would provide sufficient pressure for aerosolization of medicament but small enough to be safely handled by patients in typical environments around the home, work and school.

As to claim 4, Laube et al. as modified by Weiner et al. as discussed above also disclose a method of treating diabetes mellitus in a patient in need thereof, said method

comprising: supplying a predetermined amount of insulin formulation comprising dry powder to a hand held device (14,col.4, lines 41-50), said predetermined amount being in excess of that amount required, in the bloodstream of the patient, to produce or maintain an acceptable serum glucose level in the patient (i.e. the amount in canister 14 and in jet nebulizer disclosed at col.4, line 42 includes enough insulin for several administrations which taken together exceed any amount required to produce or maintain an acceptable serum glucose level); contacting said insulin with a compressed gas to form a cloud in said hand held device (#30,#50,#70 and col.4, lines 46-50), said cloud comprising a repeatable and controlled (i.e. 0.2U/kg body weight) amount of insulin (col.5, lines 1-12), said repeatable and controlled amount being in excess of that amount required, in the bloodstream of the patient, to produce or maintain an acceptable serum glucose level in the patient (col.5, lines 6-14); and inhaling said cloud at an inspiratory flow rate and volume (col.5, lines 53-55) adapted to deliver a portion of said cloud to the lungs of the patient, wherein an amount of said insulin in said cloud effective, in the bloodstream of the patient, to produce or maintain an acceptable serum glucose level in the patient is absorbed into the bloodstream of the patient (col.5, lines 6-14). Laube et al. as modified by Weiner et al. create an aerosol cloud of dry powder insulin within spacer device (30) prior to a patient inhaling an aerosolized dose. While Laube et al. is silent as to the particular pressure within the metered dose inhaler (14), it is submitted that the particular pressure can be arrived at through mere routine obvious experimentation and observation with no criticality seen in any particular pressure including 400psi. One or ordinary skill would recognize the need for safety when pre-

pressurizing metered dose inhalers; accordingly, pressures less than 400psi would provide sufficient pressure for aerosolization of medicament but small enough to be safely handled by patients in typical environments around the home, work and school.

As to claim 5, Laube et al. as modified by Weiner et al. (see fig.4) as discussed above, also teach mechanically supplying a predetermined amount of insulin in the form of dry powder to a given area (#30 of Laube et al.) of a hand held device.

Claim 7 is substantially equivalent in scope to claim 6 and is included in Laube et al. as modified by Weiner et al. for the reasons set forth above with respect to claim 6.

As to claim 8, Laube et al. as modified by Weiner et al. as discussed above with respect to claim 6 also teach variance in the amount of insulin actually absorbed into a patient's bloodstream (see table 2 under Peak Insulin Level). At least 1-30 Units of insulin were absorbed into each patient's bloodstream; however, it is submitted that the amount of insulin absorbed can be arrived at through mere routine obvious experimentation and observation. That is, the amount of insulin delivered to each patient and thus the amount of insulin actually absorbed (as illustrated by Laube et al.) would depend upon a variety of factors including age, weight, sex as well as other pre-existing medical conditions.

Claim 9 is substantially equivalent in scope to claim 8 and is included in Laube et al. as modified by Weiner et al. for the reasons set forth above with respect to claim 8.

Claims 10 and 11 are substantially equivalent in scope to claims 8 and 9 with the exception of the predetermined amount of insulin being 2-300 units of insulin. Since Laube et al. (col.5, lines 23-48) disclose the loss of at least 50 U within a holding

chamber, it would have been obvious to modify the amount of insulin delivered to patients to an amount which would exceed an amount necessary to produce or maintain acceptable serum glucose levels, including amounts within a range of 2-300 units to compensate for such losses. Laube et al. as modified by Weiner et al. as discussed above with respect to claim 6 also teach variance in the amount of insulin actually absorbed into a patient's bloodstream (see table 2 under Peak Insulin Level). At least 1-30 Units of insulin were absorbed into each patient's bloodstream; however, it is submitted that the amount of insulin absorbed can be arrived at through mere routine obvious experimentation and observation. That is, the amount of insulin delivered to each patient and thus the amount of insulin actually absorbed (as illustrated by Laube et al.) would depend upon a variety of factors including age, weight, sex as well as other pre-existing medical conditions.

As to claims 12 and 13, Laube et al. as discussed above, also teach determining the amount of insulin required, in the bloodstream of a patient, to produce or maintain an acceptable serum glucose level (col.3, lines 13-21).

As to claim 14, since Laube et al. (col.5, lines 23-48) disclose the loss of at least 50 U within a holding chamber, it would have been obvious to modify the amount of insulin delivered to patients to an amount which would exceed an amount necessary to produce or maintain acceptable serum glucose levels, including amounts within a range of 2-10 times an amount required to produce or maintain acceptable serum glucose levels. During typical insulin therapy of a diabetic patient the amount of insulin initially administered to diabetic patients is typically arrived at by delivering an amount which is

equivalent to the amount of insulin which is typically generated by a non-diabetic patient of the same general weight and sex and the subject patient. The amount given in subsequent administrations may be varied in dependence upon the concentration of blood glucose and upon the amount of glucose detected in the subject patient's urine. Consequently, during typical insulin therapy the amount of insulin administered to patients is arrived at through mere routine obvious experimentation and observation.

The differences between Laube et al. and claim 15 are a required amount of between 1-30 units of insulin, aerosolizing 2-10 times the amount of insulin required to produce or maintain an acceptable serum glucose level and the amount of absorbed insulin being 1-30 units.

Since Laube et al. (col.5, lines 23-48) disclose the loss of at least 50 U within a holding chamber, it would have been obvious to modify the amount of insulin delivered to patients to an amount which would exceed an amount necessary to produce or maintain acceptable serum glucose levels, including amounts within a range of 2-10 times an amount required to produce or maintain acceptable serum glucose levels. During typical insulin therapy of a diabetic patient the amount of insulin initially administered to diabetic patients is typically arrived at by delivering an amount which is equivalent to the amount of insulin which is typically generated by a non-diabetic patient of the same general weight and sex and the subject patient. The amount given in subsequent administrations may be varied in dependence upon the concentration of blood glucose and upon the amount of glucose detected in the subject patient's urine.

Consequently, during typical insulin therapy the amount of insulin administered to patients is arrived at through mere routine obvious experimentation and observation.

Claim 16 is substantially equivalent in scope to claim 15 and is included in Laube et al. as modified by Weiner et al. for the reasons set forth above with respect to claim 15.

As to claim 17, Laube et al. as discussed above, also teach repeating the administration of insulin with a second predetermined amount which is the same as or different from the first predetermined amount and is in excess of the amount of insulin required, in the bloodstream of a patient, to produce or maintain an acceptable serum glucose level (col.6, lines 44-45 and Table 2).

Claims 18-21 are substantially equivalent in scope to claim 17 with the exceptions of dosage amount of insulin and the form of insullin being dry powder. Therefore, claims 18-21 are included in Laube et al. as modified by Weiner et al. for the reasons set forth above with respect to claim 17, that is, Laube et al. teach repeating the administration of insulin with a second predetermined amount which is the same as or different from the first predetermined amount and is in excess of the amount of insulin required, in the bloodstream of a patient, to produce or maintain an acceptable serum glucose level (col.6, lines 44-45 and Table 2) and for the reasons set forth above with respect to the administration of variable amounts of insulin, that is, since Laube et al. (col.5, lines 23-48) disclose the loss of at least 50 U within a holding chamber, it would have been obvious to modify the amount of insulin delivered to patients to an amount which would exceed an amount necessary to produce or maintain acceptable serum glucose levels, including amounts within a range of 2-10 times an amount required to produce or

maintain acceptable serum glucose levels. During typical insulin therapy of a diabetic patient the amount of insulin initially administered to diabetic patients is typically arrived at by delivering an amount which is equivalent to the amount of insulin which is typically generated by a non-diabetic patient of the same general weight and sex and the subject patient. The amount given in subsequent administrations may be varied in dependence upon the concentration of blood glucose and upon the amount of glucose detected in the subject patient's urine. Consequently, during typical insulin therapy the amount of insulin administered to patients is arrived at through mere routine obvious experimentation and observation.

As to claims 22-25, Laube et al. (col.3, lines 10-21; col.7, lines 36-56) as discussed above, also determine a desired dose of insulin that, when absorbed by the patient's body will result in an acceptable serum glucose level and comparing whether the patient's blood glucose level is in an acceptable range.

3. Claims 2,6,10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laube et al. ('094) in view of Weiner et al. ('886) as applied to claims 1,3-5,7-9,11-25 above, and further in view of Blackstrom et al. ('203).

As to claim 2, Laube et al. as modified by Weiner et al. as discussed above with respect to claim 1, disclose a method of treating diabetes mellitus in a patient in need thereof, said method comprising: supplying a predetermined amount of powdered insulin (Weiner et al.) to a hand held device (14,col.4, lines 41-50), said predetermined amount being in excess of that amount required, in the bloodstream of the patient, to produce or maintain an acceptable serum glucose level in the patient (i.e. the amount in

canister 14 and in jet nebulizer disclosed at col.4, line 42 includes enough insulin for several administrations which taken together exceed any amount required to produce or maintain an acceptable serum glucose level); contacting said insulin with a compressed gas to form a cloud in said hand held device (#30,#50,#70 and col.4, lines 46-50), said cloud comprising a repeatable and controlled (i.e. 0.2U/kg body weight) amount of insulin (col.5, lines 1-12), said repeatable and controlled amount being in excess of that amount required, in the bloodstream of the patient, to produce or maintain an acceptable serum glucose level in the patient (col.5, lines 6-14); and inhaling said cloud at an inspiratory flow rate and volume (col.5, lines 53-55) adapted to deliver a portion of said cloud to the lungs of the patient, wherein a predictable and controlled quantity of insulin from said cloud is absorbed by the patient via the patient's lungs and results in the patient maintaining an acceptable serum glucose level following administration of insulin (col.5, lines 6-14).

The difference between Laube et al. as modified by Weiner et al. and claim 2 is insulin particles 7-12 microns.

Blackstrom et al., in a method for treating diabetes mellitus by administration of powdered insulin, teach particle sizes of 0.01-10 microns for the purpose of achieving deposition within a patient's lower respiratory tract (col.2, lines 15-23).

It would have been obvious to further modify the medicament in Laube et al. to make the particle sizes between 0.01-10 microns because it would have enabled deposition of the medicament within a patient's lower respiratory tract as taught by Blackstrom et al..

As to claim 6, since Laube et al. (col.5, lines 23-48) disclose the loss of at least 50 U within a holding chamber, it would have been obvious to modify the amount of insulin delivered to patients to an amount which would exceed an amount necessary to produce or maintain acceptable serum glucose levels, including amounts within a range of 2-10 times an amount required to produce or maintain acceptable serum glucose levels.

Blackstrom et al., in a method for treating diabetes mellitus by administration of powdered insulin, teach particle sizes of 0.01-10 microns for the purpose of achieving deposition within a patient's lower respiratory tract (col.2, lines 15-23).

It would have been obvious to further modify the medicament in Laube et al. to make the particle sizes between 0.01-10 microns because it would have enabled deposition of the medicament within a patient's lower respiratory tract as taught by Blackstrom et al..

Claim 10 is substantially equivalent in scope to claims 8 and 9 with the exception of the predetermined amount of insulin being 2-300 units of insulin and the size of the insulin particles being 7-12 microns. Since Laube et al. (col.5, lines 23-48) disclose the loss of at least 50 U within a holding chamber, it would have been obvious to modify the amount of insulin delivered to patients to an amount which would exceed an amount necessary to produce or maintain acceptable serum glucose levels, including amounts within a range of 2-300 units to compensate for such losses. Laube et al. as modified by Weiner et al. as discussed above with respect to claim 6 also teach variance in the amount of insulin actually absorbed into a patient's bloodstream (see table 2 under Peak Insulin Level). At least 1-30 Units of insulin were absorbed into each patient's

bloodstream; however, it is submitted that the amount of insulin absorbed can be arrived at through mere routine obvious experimentation and observation. That is, the amount of insulin delivered to each patient and thus the amount of insulin actually absorbed (as illustrated by Laube et al.) would depend upon a variety of factors including age, weight, sex as well as other pre-existing medical conditions.

Blackstrom et al., in a method for treating diabetes mellitus by administration of powdered insulin, teach particle sizes of 0.01-10 microns for the purpose of achieving deposition within a patient's lower respiratory tract (col.2, lines 15-23).

It would have been obvious to further modify the medicament in Laube et al. to make the particle sizes between 0.01-10 microns because it would have enabled deposition of the medicament within a patient's lower respiratory tract as taught by Blackstrom et al..

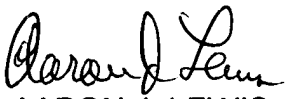
Conclusion

4. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The balance of the art is cited to show relevant methods of treating diabetes mellitus.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AARON J. LEWIS whose telephone number is (571) 272-4795. The examiner can normally be reached on 9:30AM-6:00PM M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, HENRY A. BENNETT can be reached on (571) 272-4791. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



AARON J. LEWIS
Primary Examiner
Art Unit 3743

Aaron J. Lewis
December 12, 2004